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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,691	11/12/2003	Andrew Robert Davids	674582-2001	5783

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EXAMINER	
SHAFER, SHULAMITH H	
ART UNIT	PAPER NUMBER
1647	
MAIL DATE	DELIVERY MODE
03/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/706,691	DAVIDS ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-15 and 17-78* is/are pending in the application.

4a) Of the above claim(s) *4-9,17-19 and 22-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10-15,20,21 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6 December 2007 has been entered.

The amendment received 6 December 2007 has been entered. Claims 1, 4-15, and 17-78 are pending in the instant application. Claims 1, 10 and 78 have been amended and the amendment made of record. Claims 4-9, 17-19, and 22-77 are withdrawn as being directed to a non-elected invention. Claims 1, 10-15, 20, 21 and 78 are under consideration.

It is noted that Applicant discusses Exhibit 1 and post–filing documents such as Chung et al and Moh et al in Remarks submitted 6 December 2007 (page 16, paragraphs 1-5). However, Exhibit 1 and the cited references could not be found among the papers submitted on 6 December 2007, and accordingly could not be considered.

Priority:

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on 30 April 2002. It is noted, however, that applicant has not filed a certified copy of the United Kingdom 0209884.6 application as required by 35 U.S.C. 119(b). Therefore, benefit of the foreign priority filing date is not granted.

Withdrawn Objections/Rejections

Objections:

The objections to Claims 1 and 78 are withdrawn in view of Applicant's amendment to the claims.

Rejections:

The rejection of Claims 1, 10-15, 20, and 21 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons cited in Office Action of 6 June 2007 is withdrawn in view of Applicant's amendment to the claims. New issues are addressed below.

The rejection of Claim 78 under 35 U.S.C. 103(a) as being unpatentable over Baughn *et al* (WO0240671) as applied to claim 1 in view of Ruben et al. (2002. US 6,420,526, filed 8 September 1998, the '526 patent) is rendered moot. Upon further consideration of the Baughn reference, it was found to be anticipatory of Claim 78 in addition to being anticipatory of claims 1, 10-15, 20, and 21. The Baughn et al. reference also teaches fusion proteins comprising fragments of any of SEQ ID NOs:16, 20, 22 or 26 and a heterologous protein (see discussion below).

Maintained/New Rejections and/or Objections

Double Patenting Rejection:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application

claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 15 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30, 31, and 39 of co-pending application 10/579,113.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The co-pending application claims a composition of matter comprising a polypeptide comprising an amino acid sequence recited in SEQ ID NO:20 or SEQ ID NO:22 (Claim 1), a polypeptide comprising two amino acid sequences, (a) and (b) wherein (a) is an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:20 or SEQ ID NO:22 and (b) is a heterologous amino acid sequence. These claims would encompass the isolated polypeptide recited in claim 1 and the fusion protein recited in claim 78 of the instant application. Claim 31 of SSN 10/579,113 is directed to a method of using

composition comprising a polypeptide comprising an amino acid sequence recited in SEQ ID NO:20 or SEQ ID NO:22 for diagnosis or therapy. Since no specific method steps are recited in claim 31 of the referenced application, one would interpret the claim as anticipating or rendering obvious claim 15 of the instant application, which is drawn to an isolated polypeptide comprising an extracellular domain as recited in SEQ ID NO: 22 for use in therapy or diagnosis. Thus, claims 30, 31 and 39 of SSN 10/579,113 anticipate or render obvious claims 1, 15 and 78 of the instant invention.

This is a provisional double patenting rejection since the conflicting claims have not, in fact, been patented.

35 U.S.C. § 112, Second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10-15, 20, 21 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to recite “an isolated polypeptide comprising an extracellular domain as recited in SEQ ID NO:22". It is unclear what is meant by “comprising an extracellular domain as recited in SEQ ID NO:22”; it is unclear if applicant intends the extracellular domain to comprise or consist of SEQ ID NO:22, or some unspecified part thereof. Furthermore, part (ii) of the claim recites “consists of the amino acid sequence as recited in SEQ ID NO:20 or SEQ ID NO:22” which could be interpreted as being drawn to a polypeptide consisting of SEQ ID NO:20 or 22. However, part (iii) of the claim is drawn to a “fusion protein according to (i) or (ii) or comprising a *fragment* of a polypeptide according to (i) or (ii). It is unclear how a fragment may comprise or consist of the amino acid sequence as recited in SEQ ID NO:16 or SEQ ID NO:26 or consist of the amino acid sequence of SEQ ID NO:20 or SEQ ID NO:22.

Claim 13 is vague and indefinite in reciting "A compound that either increases or decreases the level of expression or activity of a polypeptide.....without inducing any of the biological effects of the polypeptide" It is unclear how one can increase the biological activity of a polypeptide without inducing biological effects of said peptide.

Claims 10-12, 14, 15, 20, and 78 are included in the rejection as depending from rejected claims.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 1, 10-15, 20, 21 and 78 under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a full length polypeptide comprising or consisting of SEQ ID NOs:16, 20, 22 or 26 or a fusion polypeptide comprising a polypeptide which comprises or consists of the amino acid sequence as recited in SEQ ID NOs:16, 20, 22 or 26 fused to a heterologous polypeptide that has an activity that is an antagonist of TNF-alpha, IL-4, IL-6 and or IL-2 does not reasonably provide enablement commensurate with the full scope of the claim is maintained for reasons of record and for reasons set forth below.

Claim 1, the independent claim of the instant invention has been amended and is now drawn to an isolated polypeptide "comprising an extracellular domain as recited in SEQ NO:22 which polypeptide: (i) comprises or consists or the amino acid sequence as recited in SEQ ID NO:16 or SEQ ID NO:26 or (ii) consist of the amino acid sequence as recited in SEQ ID NO:22 or SEQ ID NO:22". Section (iii) is drawn to a fusion protein comprising a polypeptide according to (i)

or (ii) or comprising a fragment of a polypeptide according to (i) or (ii). Section (iii) can reasonably be interpreted as being drawn to a fusion protein comprising a fragment of any one of SEQ ID NOs: 16, 20, 22, or 26 fused to a heterologous polypeptide, since the language of the preamble to claim 1 is indefinite (See above discussion). It is also noted that the claim no longer recites any required activity of function for the fusion protein. Accordingly, the specification neither provides adequate guidance as to how to *make* functional species, nor how to *use* those that are not, which would be expected to be the majority of species.

There is no guidance presented in the specification as to how to make and/or use fusion proteins comprising fragments of any one of SEQ ID NOs:16, 20, 22 or 26 fused to heterologous polypeptides. Insufficient teaching is presented as to which fragments of the full length proteins must be retained in order to arrive at a functional protein. While one of skill in the art may construct a fusion protein comprising any given fragment of a protein, it would require undue experimentation to determine which fragments would maintain the functioning envisioned in the claims of the instant invention (for example, claims 10 and 15).

Applicant traverses the rejection (page 15 of Response of 6 December 2007). The reasons for the traversal are:

a. The specification discloses that functional polypeptides can be identified using the Inpharmatica Gene Threader

b. The claims now require that the polypeptide, at a minimum, must comprise the extracellular domain as recited in SEQ ID NO:22.

c. Exhibit 1 presents additional data that demonstrates the necessity of the recited extracellular domain of SEQ ID NO:22 in the claimed polypeptides.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons

In response to a: As previously stated, the Inpharmatica Gene Threader system is acknowledged by applicants as being an in-house system developed by Inpharmatica. This system did not appear to be publicly available at the time of filing of the instant invention. Therefore, one of ordinary skill in the art could

not rely upon the Gene Threader system, in addition to guidance in the specification, or the teachings in the art to make and use fusion proteins comprising fragments of any one of SEQ ID NOs: 16, 20, 22 and 26

In response to b: The language of the claim is indefinite. One can reasonably interpret section (iii) to be directed to a fusion protein comprising a fragment of any one of SEQ ID NOs: 16, 20, 22 and 26. Thus, it would require undue experimentation to determine which fragments of the above listed sequences could be used to construct a functional fusion protein.

In response to c: As stated above, Exhibit 1 could not be found among the papers submitted on 6 December 2007. Therefore, evidence presented in Exhibit 1 could not be evaluated.

The rejection of Claims 15, 20 and 21 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide or a fusion protein comprising a full length polypeptide for use in therapy for treatment of fulminant hepatitis in a mouse model does not reasonably provide enablement for a polypeptide or fusion protein comprising a full length polypeptide for use in therapy and diagnosis in an inflammatory disease, an autoimmune disease, any generic liver disease or liver failure is maintained for reasons of record and for reasons set forth below.

Applicant traverses the rejection (page 16 of Response of 6 December 2007). The reasons for the traversal are:

a. Example 1 from Exhibit 1demonstrates how INSP052 modulates cytokine expression in a mouse model used as a model for fulminant hepatitis treatment

b. Example 2 from Exhibit 1 teaches INSP052EC is shown to reduce ear swelling in a model of contact hypersensitivity and thus is useful in treating T cell mediated inflammation of the skin.

c. INSP052 is identical to a protein described in the literature as Hepatocyte cell adhesion molecule (hepaCAM). Post filing publications provide

further evidence of the role of INSP052 in wound healing, cell adhesion and growth control.

Applicant's arguments have been fully considered but are not found to be persuasive. Evidence submitted in Exhibit 1, including post-filing date references cannot be evaluated, as Exhibit 1 could not be found among papers submitted on 6 December 2007.

Applicant asserts that the specification teaches the skilled person to identify fragments that contain an immunoglobulin domain (page 8 of specification) and the functional importance of this domain (page 16, lines 4-9); data presented confirm that extracellular fragments retain activity of the full length protein. This is not persuasive; while the specification teaches that INSP052 proteins comprise immunoglobulin domain-containing cell surface recognition molecules (page 8), lines 9-10, the specification does not provide teachings as to identifying fragments comprising an immunoglobulin domain. While one may appreciate the importance of an immunoglobulin domain, insufficient guidance is presented to allow one to identify which fragments comprise said domains and to be able to construct a functional fusion protein.

Applicant reminds examiner that fragments consisting of exons 2 and 3 of the INSP052 polypeptide as they are specifically disclosed on pages 10 and 11. Applicant is arguing limitations not recited in the claims since the claims are not directed to fragments comprising INSP052 exon 2 polypeptide (SEQ ID NO:4) or fragments comprising INSP052 exon 3 polypeptide (SEQ ID NO:6).

The rejection of Claims 1, 10-15, 20 and 21 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record and reasons set forth below.

Applicant traverses the rejection (page 17 of Response of 6 December 2007). The reasons for the traversal are:

Amended claims now require that the isolated polypeptide comprises an extracellular domain as recited in SEQ ID NO:22; the claimed isolated

polypeptide must now, at a minimum, comprise an extracellular domain as recited in SEQ ID NO:22.

Applicant's arguments have been fully considered but are not found to be persuasive. As previously discussed, the claim language of claim 1 is indefinite. Therefore, claim 1(iii) and claims depending from claim 1, could reasonably be interpreted to recite fusion proteins comprising fragments of any one of SEQ ID NOs: 16, 20, 22 and 26. The claims do not require that the polypeptide or fragment thereof possess any disclosed distinguishing feature or specific activity.

Therefore, only isolated polypeptides comprising fusion proteins comprising the full length sequence of SEQ ID NOs: 16, 20, 22, or 26 fused to a heterologous polypeptide but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The rejection of Claims 1, 10-15, 20, and 21 under 35 U.S.C. 102(a) and (e) as being anticipated by Baughn, *et al* (WO0240671, publication date 23 May 2002, priority claimed to provisional application 60/249,645, 16 November 2000, cited in previous Office Action) is maintained for reasons of record and for reasons set forth below and is now applied to claim 78.

In addition to the teachings of Baughn et al set forth in previous office actions, the reference teaches fusion proteins comprising an IGFSP protein ligated to a heterologous protein sequence (page 39, lines 19-21, fusion proteins comprising an IGFSP protein and a short cationic N-terminal portion from the HIV

Tat-1 protein (page 54, lines 12-13), and fusion proteins comprising IGFSP protein and glutathione S-transferase, or a peptide epitope tag (page 78, lines 5-10). Thus, in addition to anticipating the limitations Claims 1, 10-15, 20, and 21, the reference also anticipates the limitations of Claim 78.

Applicant traverses the rejection (page 18 of Response of 6 December 2007). The reasons for the traversal are:

a. Pending claims require that the isolated polypeptide comprises an extracellular domain of SEQ ID NO:22

b. Baughn et al. do not disclose the existence a polypeptide comprising an an extracellular domain as recited in SEQ ID NO:22

Applicant's arguments have been fully considered but are not found to be persuasive.

As noted above, the claim language is indefinite. Claim 1 could reasonably be interpreted to be drawn to a polypeptide comprising SEQ ID NO:22, or to a fusion protein comprising a fragment of any one of SEQ ID NOs: 16, 20, 22 and 26.

In response to a: The sequence disclosed by Baughn et al (IGFSP-4) comprises SEQ ID NOs:20 or 22 of the instant invention. Additionally, Baughn et al. teach a polypeptide (AAE14784) comprising a sequence which is 100% identical to amino acids 1-291 of SEQ ID NO:16 of instant invention. Thus, fusion proteins comprising fragments of SEQ ID NO:16 are taught by Baughn et al. Furthermore, this sequence comprises a sequence which is 100% identical to amino acids 1-258 of SEQ ID NO:26 of the claimed invention; fusion proteins comprising fragments of SEQ ID NO:26 are also taught by the reference.

In response to argument b: While the teachings of Baughn et al do not specifically identify IGFSP-4 as comprising an extracellular domain of SEQ ID No:22, the IGFSP-4 taught by Baughn et al. is a protein comprising SEQ No:22; thus the IGFSP-4 taught by the reference would of necessity comprise the extracellular domain of SEQ ID NO:22.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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